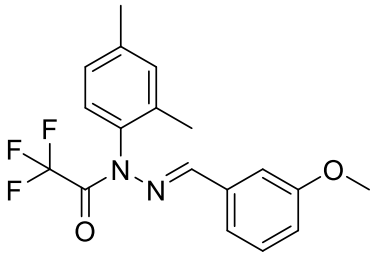
Product data sheet

MedKoo Cat#: 522384 Name: J147 CAS#: 1146963-51-0 Chemical Formula: $C_{18}H_{17}F_3N_2O_2$ Exact Mass: 350.12421 Molecular Weight: 350.34	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

J147 is a potent neuroprotective and neurotrophic compound. J147 protects against neurotoxicity in cortical neurons in vitro (EC50 = 25 - 200 nM). J147. J147 reverses cognitive impairment in aged Alzheimer's disease mice. J147 is an exciting new compound that is extremely potent, safe in animal studies and orally active. J147 is a potential AD therapeutic due to its ability to provide immediate cognition benefits, and it also has the potential to halt and perhaps reverse disease progression in symptomatic animals as demonstrated in these studies.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	68.0	194.10

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.85 mL	14.27 mL	28.54 mL
5 mM	0.57 mL	2.85 mL	5.71 mL
10 mM	0.29 mL	1.43 mL	2.85 mL
50 mM	0.06 mL	0.29 mL	0.57 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Prior M, Dargusch R, Ehren JL, Chiruta C, Schubert D. The neurotrophic compound J147 reverses cognitive impairment in aged Alzheimer's disease mice. Alzheimers Res Ther. 2013 May 14;5(3):25. doi: 10.1186/alzrt179. PMID: 23673233; PMCID: PMC3706879.

In vivo study

1. Currais A, Huang L, Goldberg J, Petrascheck M, Ates G, Pinto-Duarte A, Shokhirev MN, Schubert D, Maher P. Elevating acetyl-CoA levels reduces aspects of brain aging. Elife. 2019 Nov 19;8:e47866. doi: 10.7554/eLife.47866. PMID: 31742554; PMCID: PMC6882557.
2. Prior M, Dargusch R, Ehren JL, Chiruta C, Schubert D. The neurotrophic compound J147 reverses cognitive impairment in aged Alzheimer's disease mice. Alzheimers Res Ther. 2013 May 14;5(3):25. doi: 10.1186/alzrt179. PMID: 23673233; PMCID: PMC3706879.

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7. Bioactivity

Biological target:

J-147 is a neuroprotective agent for cognitive enhancement that inhibits monoamine oxidase B (MAO B) and the dopamine transporter with EC50 values of 1.88 μM and 0.649 μM, respectively.

In vitro activity

Additional support for an effect of J147 on neurotrophic pathways came from a study with HT22 cells. HT22 is a nerve cell line derived from mouse brain and is widely used to study nerve cell physiology. To examine the effect of J147 on gene expression, a DNA microarray study probed expression of over 34,000 named mouse genes. J147 increased transcription factor Egr3 mRNA expression 8-fold following one hour of treatment, while Ngf mRNA was up-regulated 2.8-fold (Table1). Also up-regulated was mRNA from another member of the Egr family, Egr1, with a 2.5-fold increase and mRNA from a member of the Spred family, Spred2, with a 2.7-fold increase. J147 did have an effect on other genes. To determine the biological consequences of J147 induction of neurotrophin expression, it was asked if conditioned media (CM) prepared from HT22 cells treated with J147 could stimulate neurite outgrowth in PC12 cells. Both conditioned medium from J147 treated cells (Figure3G,3G, middle right panel) and NGF treated cells promoted neurite outgrowth (Figure3G,3G, top right panel), while control medium did not (Figure3G,3G, top and middle left panels). This effect was reduced by anti-NGF anti-sera suggesting that J147 releases neurotrophins with an effect on neurites similar to those released by NGF (Figure3G,3G, bottom panels).

Reference: Alzheimers Res Ther. 2013; 5(3): 25. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3706879/

In vivo activity

Both male and female huAPP/PS1 mice were aged to 20 months. At this time, the mice were randomly assigned to one of two groups: 11 mice were fed normal food and 13 mice were fed the same diet but also containing 200 ppm J147. Following three months of treatment, all mice were analyzed for spatial memory performance by the two-day water maze (Figure1A), disinhibition phenotype by the elevated plus maze (Figure1B), and contextual and cued memory by a fear conditioning assay (Figure1C and 1D, respectively). Results from Day 1 indicate no defects in AD or AD + J147 in the ability to swim or see as both have similar escape latency. Results from this two-day water maze show that AD mice take considerably longer to find the hidden platform on Day 2 than AD mice treated with J147 for three months (Figure1A), demonstrating that J147 significantly improved the spatial navigational memory in aged, transgenic AD mice. The data demonstratse that aged transgenic AD mice do indeed spend more time in the open arm, a phenotype that was completely rescued by treatment with J147 for three months (Figure1B). AD mice alone spent significantly less time freezing in response to the context associated with the aversive stimulus in our experiment, indicating that they did not remember the context, a phenotype that was rescued by treatment with J147 (Figure1C). Results from these behavioral assays show that J147 has the ability to rescue the cognitive decline and disinhibition phenotype associated with AD when administered at an extremely late stage in the disease progression when pathology is already far advanced.

Reference: Alzheimers Res Ther. 2013; 5(3): 25. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3706879/